AN INTERVIEW WITH...

Rasha Al-Lamee, MA, MBBS, FRCP, PhD

Dr. Al-Lamee discusses the importance of research in cardiology care, thoughts on the ORBITA and EXCEL trials, and the effect of COVID-19 on the clinical trial landscape.

As a leading clinical academic, research is a crucial aspect of your work. Early last year, the Academy of Medical Sciences published a report about needing to protect and strengthen health research in the United Kingdom, highlighting the connection between health care settings active in research and better patient outcomes and care, as well as calling for the National Health Service (NHS) to give staff protected time for research.[1] Why is research so critical for cardiology care? What advice do you have for young cardiologists who want to prioritize research?

I think embedding research into clinical cardiology care is absolutely crucial to improving patient outcomes for individuals and the wider population. I often tell our research patients that involvement in research means that they learn so much more about their disease and we learn so much more about them. In a busy clinical service, we try our hardest to give personalized care to all, but it's not always easy. Participation in a research trial allows patients to have more one-on-one time with a clinical team. Beyond the individual, I think departments that are active in research are more agile. They have access to new data, devices, and approaches to management. Here in the United Kingdom, we have a unique environment for attaining research excellence in health sciences. We have the opportunity to deliver truly practice-changing research with the NHS, multiple charities and government bodies that invest in research, policy makers who are committed to evidence-based decision-making, and world-leading academic institutions that work in partnership with NHS trusts across the country.

I encourage young cardiologists to find a way to integrate research into their clinical careers. For some, this will be pursuing a part-academic, part-clinical path. For others, it will mean being involved in research while working in a full-time clinical position. It doesn't matter which path you choose—both are absolutely fundamental to making research a success.

Importantly, I think many physicians are concerned that adding research to their responsibilities will just give them work to do. The truth is, it does add to your to-do list, but it also enhances job satisfaction. It means you can meet fantastic patients and have the chance to get to know them very well and can build up a national and international network of interesting and dynamic colleagues. Ultimately, research adds variety and interest to your job, allowing you to constantly learn and adapt your clinical practice.

Much of your career is centered on the development and recruitment of clinical trials. What is your philosophy for identifying which questions are worth pursuing in a trial and designing and conducting said trials?

I was told many years ago by my PhD supervisor, Professor Darrel Francis, that the questions worth answering are often the simplest ones. Importantly, I also learned that we should never assume we cannot ask the same questions again and try to answer them in a new way.

I like to design trials that address questions important to patients. In the end, they are the ones who commit their time and energy to help us with our research, so we must make sure our trials can inform our understanding of their disease and potentially change our practice for the better.

One aspect of my research that has evolved is the degree to which I now involve patients in designing new trials. It's easy to pay lip service to patient and public involvement; but I have found that if you take it seriously, you come out of every session with new research questions and novel thoughts on how to answer them. For example, often when we are testing a therapy, our idea of the primary outcome as clinicians is totally different from what our patients think is most important.

(Continued on page 64)

(Continued from page 66)

The publication of the ORBITA trial, for which you were Principal Investigator, was a landmark for your career—as well as the subject of much discussion in the cardiology world. How did you go about addressing the sometimes controversial responses? Would you do anything differently if you could go back and redo the trial?

Controversy is always difficult to deal with, and I don't know if I will ever master the perfect approach. I think the hardest part is learning not to take criticism personally, especially when you have put a lot of time and energy into your work! My way of handling controversy has always been to keep explaining the data and what I believe they show. Sometimes there is a tendency to overreach and make sweeping statements based on your own data. I have tried as hard as I can to not do that.

In terms of going back again, I really don't think I would change much. It's so easy to retrospectively judge a trial based on its results, especially if we wish they were different. That's unfortunately not how life goes. We have to make choices and then stand by them, regardless of the outcome. Most of the decisions we made in designing ORBITA were based on trying to plan a novel trial that would attempt to answer an important scientific question ethically. As the first placebo-controlled trial of percutaneous coronary intervention (PCI), we needed to make sure it was ethical and acceptable to our patients and coinvestigators. I don't think I'd do much differently if I could go back, except maybe prepare our whole team and myself much more for the emotional rollercoaster of publishing a trial with unpopular results!

You've shared that ORBITA underlined the need for blinding and a placebo control when studying interventions with subjective endpoints,[2] and building on the findings from ORBITA, the ORBITA-2 trial is currently underway. What are your main goals for that trial? Are there other areas of intervention you hope to study in placebo-controlled trials next?

ORBITA-2 is indeed underway at many centers across the United Kingdom with the help of many fantastic colleagues who participated in the first ORBITA trial, as well as new teams that have joined us. Designing this trial was much easier because we could build on what we already learned and try to fill in the gaps in our knowledge. ORBITA-2 is being run by my PhD student Alexandra Nowbar. It once again compares PCI to placebo in patients with stable angina, but this time patients are on real-world medical therapy and can have single- or multivessel disease, and the primary endpoint encompasses symptom assessment on a smartphone application. We will see what it shows in a few years' time!

There are some other exciting placebo-controlled trials underway with my other PhD students Christopher Rajkumar and Michael Foley, who are running ORBITA-STAR and ORBITA-COSMIC, respectively. They are studying other interesting aspects of symptom evaluation and novel diagnostic and treatment tools in stable coronary artery disease, so the future pipeline is incredibly exciting.

Some of your recent research has been focused on evaluating data and outcomes from trials that studied PCI for patients with coronary artery disease—specifically, COURAGE, ORBITA, and ISCHEMIA. What do you think should be the next step for research in this area?

I think we need to connect the dots between symptoms, ischemia, and angiographic stenosis. Our work will focus on trying to understand where links exist and where they don't. Stable coronary artery disease is not going away anytime soon, so we need to work out what is best for our patients in terms of diagnosis and treatment.

What are your thoughts on the EXCEL trial and the current state of the data?

I couldn't understand the controversy at the time, and I suspect that some of the extreme polarity of opinion and sensationalism of the story was somewhat inflated by the media. I think we have seen lots of evidence that mortality is very similar with PCI or coronary artery bypass grafting (CABG) for left main stem disease. Procedural myocardial infarction rates clearly depend on the definitions used. Once again, we saw a debate driven by controversy. We have to be careful not to make sweeping statements and to recognize that PCI may be the best option for some patients, and CABG may be the best option for others. That's why our heart team discussions are so important. Most of us interventional cardiologists work very well with our cardiothoracic surgeons and make important decisions together on the most appropriate management for our

patients all the time. Let's face it, many of the patients we discuss there would never have made it into any randomized controlled trial.

Now that we're a year from the start of the COVID-19 pandemic in the United Kingdom, what does the research landscape in your field look like? What lasting effects on trials do you expect to see in the next months or years as a result of the pandemic?

Clearly this year has been crazy; but in the fullness of time, I think we will be able to reflect and realize that despite lots of challenges, there were some positives. We will have to do that, otherwise it will be impossible to move on!

The first wave of COVID-19 in the United Kingdom was a difficult time for clinical research. Most non-COVID clinical trials were ordered to stop, and it took some time for us to restart many trials across the country. Unfortunately, just as life started to get back to normal, the second big wave arrived and eclipsed the first in many areas of the country. I think we are going to see that the vast majority of publications in the coming years will include a description of what effects COVID-19 had on the trial and how protocols were adapted to cope with the new landscape.

However, a real triumph has been how scientific research pivoted to understanding and treating a new disease process. What has been achieved in a short space of time with the RECOVERY trial and vaccine research is quite unbelievable and is a real testimony to the power of scientific endeavor.

We should never forget that cardiovascular disease has not gone away, and cardiovascular research will always need to be a priority. I am sure we can find our way back and that there is a will to get our research on track as quickly as possible.

Can you tell us about your role as Co-Chair of the European Association of Percutaneous Cardiovascular Interventions (EAPCI) Patient Initiatives Committee and the goals you have for this position?

I was delighted to be asked to cochair this panel along with the committee chair Robert Byrne. We have a fantastic group of fellow committee members who meet regularly to discuss new and ongoing projects. We hope that over the next 2 years, our group will develop new initiatives that will be directed toward improving many aspects of patient care. Our first priorities are targeted at novel assessments of patient-related outcome measures, gathering data on consent processes for interventional procedures across Europe, and new techniques to inform our patients about the procedures they are scheduled to undergo. I'm looking forward to seeing what we achieve in conjunction with the fantastic team at EAPCI. ■

1. The Academy of Medical Sciences. Transforming health through innovation: integrating the NHS and academia. Accessed February 18, 2021. https://acmedsci.ac.uk/file-download/23932583
2. Foley M, Al-Lamee R. Making sense of ORBITA and ISCHEMIA. Cardiac Interv Today. 2020;14:40-43.

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